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NEWS 26	APR 28	ENCOMPLIT/ENCOMPLIT2 search fields enhanced
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                  limits for exact sequence match searches and
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=> s screen?
L1     1749819 SCREEN?

=> s l1 and antibod?
L2      143903 L1 AND ANTIBOD?

=> s l2 and glycospecific
L3           4 L2 AND GLYCOSPECIFIC

=> s l3 and human TSH
L4           0 L3 AND HUMAN TSH

=> s l2 and human TSH
L5          79 L2 AND HUMAN TSH
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=> s l5 and recombinant
L6          22 L5 AND RECOMBINANT

=> s l6 and sialylated
L7           0 L6 AND SIALYLATED

=> s l6 and branched
L8           0 L6 AND BRANCHED

=> s l6 and recombinant TSH
L9           5 L6 AND RECOMBINANT TSH

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10           2 DUP REMOVE L9 (3 DUPLICATES REMOVED)

=> d l10 1-2 cbib abs

L10  ANSWER 1 OF 2     MEDLINE on STN                    DUPLICATE 1
1996407409.    PubMed ID: 8811462.   Epitope mapping of a recombinant
     human TSH receptor extracellular domain: identification
     of a predominant epitope using animal sera. Hunt N; Willey K P; Abend N;
     Northemann W; Leidenberger F A. (Institute for Hormone and Fertility
     Research, University of Hamburg, Germany. ) Journal of clinical laboratory
     analysis, (1996) Vol. 10, No. 4, pp. 193-204.  Journal code: 8801384.
     ISSN: 0887-8013. Pub. country: United States. Language: English.
AB   The extracellular domain of the TSH receptor (TSHR-561, amino acids
     #78-389) was expressed as a hexa-histidine fusion protein in bacteria.
     The recombinant protein was purified to homogeneity and used to
     immunize porcine and ovine species.  High titre antibodies were
     obtained from both species that recognized the recombinant
     protein in Western blot analysis but failed to interfere with the TSH
     radio receptor assay.  An epitope library was constructed and
     screened with affinity purified ovine and porcine antisera and
     detected a number of positive clones.  Sequence analysis revealed that all
     of the epitopes contained sequences derived from the carboxyl terminus of
     the recombinant immunogen.  One clone defined an epitope
     covering 16 amino acids from the carboxyl terminus and was the common
     epitope found in all of the other clones.  Western blot screening
     of a large panel of Graves' sera with recombinant TSH
     receptor protein identified one patient sera that also recognized linear
     epitopes in the TSHR-561 protein.  Experimentation demonstrated that the
     linear epitope recognized by this human sera was identical to the sequence
     recognised by the animal antisera.  This sequence is unique to the TSH
     receptor and will be useful in further studies to analyze the TSH receptor
     protein.

L10  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
1990:453366   Document No. 113:53366  Original Reference No. 113:8913a,8916a
     Cloning, sequencing and expression of the human thyrotropin (TSH)
     receptor:  evidence for binding of autoantibodies.  Libert, Frederick;
     Lefort, Anne; Gerard, Catherine; Parmentier, Marc; Perret, Jason; Ludgate,
     Marian; Dumont, Jacques E.; Vassart, Gilbert (Fac. Med., Univ. Libre
     Brussels, Brussels, 1070, Belg.).  Biochemical and Biophysical Research
     Communications, 165(3), 1250-5 (English) 1989.  CODEN: BBRCA9.  ISSN:
     0006-291X.
AB   A human thyroid cDNA library was screened by hybridization with
     a dog TSH receptor (TSHr) cDNA.  Sequencing of the resulting clones
     identified a 2292-residue open reading frame encoding a 744-amino acid
     mature polypeptide presenting 90.3% similarity with the dog TSHr.  Two
     major transcripts (4.6 and 4.5 kb) were identified in the human thyroid
     which suggests that alternative splicing could generate multiple forms of
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human TSHr. Transfection of the coding sequence in COS-7 cells conferred to a membrane preparation of these cells the ability to bind specifically TSH. TSH binding was completely displaced by Ig prepns. from patients with idiopathic myxedema.

=> s l2 and human TSR
L11 0 L2 AND HUMAN TSR

=> s l2 and TSR
L12 4 L2 AND TSR

=> dup remove l12
PROCESSING COMPLETED FOR L12
L13 4 DUP REMOVE L12 (0 DUPLICATES REMOVED)

=> d l13 1-4 cbib abs

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
2007:999439 Document No. 147:336350 Stem cell factor-like protein SCFA1, its protein and cDNA sequences, and therapeutic uses in modulating gastrointestinal and oral epithelial cell proliferation. Emtage, Peter C. R.; Funk, Walter (Nuvelo, Inc., USA). PCT Int. Appl. WO 2007100357 A2 20070907, 119pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-US39266 20061006. PRIORITY: US 2005-724908P 20051007.
AB Methods for stimulating epithelial cell proliferation and for treating oral and gastrointestinal disorders are described. The methods use compns. comprising stem cell factor-like protein A1 (SCFA1) polypeptides and polynucleotides, including human protein and cDNA sequences. SCFA1, also known as hPWTSR and R-spondin 3, is a member of the thrombospondin type 1 repeat (**TSR**) superfamily. SCFA1 contains predicted signal peptide, 2 furin-like domains and a thrombospondin type 1 domain (TSP1).

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
2005:429525 Document No. 142:477114 DNA molecules and polypeptides of glycosyltransferases and enzymes involved in biosynthesis of deoxysugars from Streptomyces and Saccharopolyspora, their sequences and use in glycosylation of various small molecules, such as spinosyn. Trefzer, Axel; Green, Brian D.; Bibb, Mervyn; Mason, Dylan (Diversa Corporation, USA). PCT Int. Appl. WO 2005044979 A2 20050519, 226 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US25015 20040804. PRIORITY: US 2003-492781P 20030804; US 2003-515950P 20031029.
AB The invention provides a novel technol. for glycosylation of natural small mol. products using genetically engineered strains of bacteria. The invention relates that the in vivo glycosylation system expresses a

heterologous glycosyltransferase and enzymes involved in the biosynthesis of deoxysugars, which is capable of glycosylating a suitable substrate, which can be added to a culture broth. The invention also provides glycosylated derivs. of spinosyn, erythromycin, tetracycline, rifampicin, daunorubicin, mithramycin, rapamycin, FK520, FK506, amphotericin, tylosin, and/or avermectin using said disclosed glycosylation system and transformed bacteria. The invention further provides DNA and amino acid sequences of various glycosyltransferases and enzymes involved in biosynthesis of deoxysugars from Streptomyces and Saccharopolyspora, and the use of these in production of genetically engineered bacteria for glycosylating small mols. The invention also relates that said DNA sequences encode enzymes involved in biosynthesis of deoxysugar including enzymes having the following activities: nucleodidyl transferase, 4,6-dehydratase, 3,5-epimerase, 4-ketoreductase, 2,3-dehydratase, and 3-ketoreductase activities. Still further, the invention provides: (a) methods for producing said recombinant enzymes; (b) use of glycosylated spinosyn and pseudoaglycone derivs. in production of insecticides, disinfectants and pharmaceutical compns.; and (c) primers and probes specific for disclosed DNA sequences. Finally, the invention provides: (a) various methods for production of modified nucleic acid mols. encoding glycosyltransferases and enzymes involved in biosynthesis of deoxysugars from Streptomyces and Saccharopolyspora and (b) chimeric proteins comprising said glycosyltransferases and enzymes involved in biosynthesis of deoxysugars and a heterologous protein.

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN

2003:261865 Document No. 138:268316 Virulent gene products of Salmonella typhimurium and their therapeutic uses thereof. Dougan, Gordon (Microscience Limited, UK). PCT Int. Appl. WO 2003027140 A2 20030403, 20 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB4333 20020926. PRIORITY: GB 2001-23170 20010926.

AB The present invention is based on the discovery of genes in Salmonella typhimurium, the products of which are implicated in virulence and colonization. A comparison of genes that are inactive in a non-pathogenic microorganism but which are active in a related pathogenic microorganism has identified genes which may be used in therapy or diagnosis. Accordingly, peptides encoded by a gene from S. typhimurium that corresponds to any of those listed in Table 1, can be used in therapy or diagnosis. The peptides have many therapeutic uses for treating Salmonella infections, including use in vaccines for prophylactic application.

L13 ANSWER 4 OF 4 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

2000:815242 The Genuine Article (R) Number: 367YQ. Subcommissural organ/Reissner's fiber complex: Characterization of SCO-spondin, a glycoprotein with potent activity on neurite outgrowth.
Meiniel A (Reprint). Fac Med, Lab Biochim Med, 28 Pl Henri Dunant, F-63001 Clermont Ferrand, France (Reprint). Gobron S; Creveaux I; Meiniel R; Didier R; Herbet A; Bamdad M; El Bitar F; Dastugue B. Fac Med, Lab Biochim Med, F-63001 Clermont Ferrand, France; INSERM, U384, Clermont Ferrand, France.
GLIA (NOV 2000) Vol. 32, No. 2, pp. 177-191. ISSN: 0894-1491. Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In the developing vertebrate nervous system, several proteins of the thrombospondin superfamily act on axonal pathfinding. By successive **screening** of a SCO-cDNA library, we have characterized a new member of this superfamily, which we call SCO-spondin. This extracellular matrix glycoprotein of 4,560 amino acids is expressed and secreted early in development by the subcommissural organ (SCO), an ependymal differentiation located in the roof of the Sylvian aqueduct. Furthermore, SCO-spondin makes part of Reissner's fiber (RF), a thread-like structure present in the central canal of the spinal cord. This novel protein shows a unique arrangement of several conserved domains, including 26 thrombospondin type 1 repeats (**TSR**), nine low-density lipoprotein receptor (LDLr) type A domains, two epidermal growth factor (EGF)-like domains, and N- and C-terminal von Willebrand factor (vWF) cysteine-rich domains, all of which are potent sites of protein-protein interaction. Regarding the huge number of **TSR**, the putative function of SCO-spondin on axonal guidance is discussed in comparison with other developmental molecules of the CNS exhibiting **TSR**. To correlate SCO-spondin molecular feature and function, we tested the effect of oligopeptides, whose sequences include highly conserved amino acids of the consensus domains on a neuroblastoma cell line B 104. One of these peptides (WSGWSSCSRSCG) markedly increased neurite outgrowth of B 104 cells and this effect was dose dependent. Thus, SCO-spondin is a favorable substrate for neurite outgrowth and may participate in the posterior commissure formation and spinal cord differentiation during ontogenesis of the central nervous system. (C) 2000 Wiley-Liss, Inc.

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=> s l2 and carbohydrate dependent
L14         23 L2 AND CARBOHYDRATE DEPENDENT

=> s l14 and sialyated
L15          0 L14 AND SIALYATED

=> s l14 and sialylation
L16          0 L14 AND SIALYLATION

=> dup remove l14
PROCESSING COMPLETED FOR L14
L17           5 DUP REMOVE L14 (18 DUPLICATES REMOVED)

=> d l17 1-5 cbib abs

L17  ANSWER 1 OF 5     MEDLINE on STN                    DUPLICATE 1
2008277026.    PubMed ID: 18400317.   Antigenic differences within the
     Cryptosporidium hominis and Cryptosporidium parvum surface proteins P23
     and GP900 defined by monoclonal antibody reactivity. Sturbaum
     Gregory D; Schaefer Deborah A; Jost B Helen; Sterling Charles R; Riggs
     Michael W. (CH Diagnostic & Consulting Service Inc, Berthoud, CO 80513,
     USA.. gsturbaum@chdiagnostic.com) . Molecular and biochemical
     parasitology, (2008 Jun) Vol. 159, No. 2, pp. 138-41.  Electronic
     Publication: 2008-03-04. Journal code: 8006324. ISSN: 0166-6851. Pub.
     country: Netherlands. Language: English.
AB   The biological basis for the specificity of host infectivity patterns of
     Cryptosporidium spp., in particular C. hominis and C. parvum, has yet to
     be fully elucidated.  Comparison of the C. parvum and C. hominis P23 and
     GP900 predicted amino acid sequences revealed 3 differences in P23 and 4
     and 17 differences in GP900 domains 1 and 5, respectively.  Using
     monoclonal antibodies developed against the surface
     (glyco)proteins P23 and GP900 of the C. parvum Iowa isolate, solubilized
     glycoprotein from three C. hominis isolates was screened for
     reactivity using Western immunoblots.  One of ten P23 MAbs and three of 21
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GP900 MAbs were not reactive with any of the three C. hominis isolates. The non-reactive P23 MAb binds to a peptide epitope, while the non-reactive GP900 MAbs bind to either carbohydrate/**carbohydrate -dependent** or peptide epitopes of C. parvum. These results demonstrate phenotypic differences between C. hominis and C. parvum within two (glyco)proteins that are involved in parasite gliding motility and attachment/invasion.

L17 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2

2007494126. PubMed ID: 17630779. Fine epitope mapping of monoclonal **antibody** 5F1 reveals anticatalytic activity toward the N domain of human angiotensin-converting enzyme. Danilov Sergei M; Watermeyer Jean M; Balyasnikova Irina V; Gordon Kerry; Kugaevskaya Elena V; Elisseeva Yulia E; Albrecht Ronald F 2nd; Sturrock Edward D. (Department of Anesthesiology, University of Illinois at Chicago, Chicago, Illinois 60612, USA.. danilov@uic.edu) . Biochemistry, (2007 Aug 7) Vol. 46, No. 31, pp. 9019-31. Electronic Publication: 2007-07-14. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB Angiotensin I-converting enzyme (ACE, peptidyl dipeptidase, EC 3.4.15.2) is a key enzyme in cardiovascular pathophysiology. A wide spectrum of monoclonal **antibodies** to different epitopes on the N and C domains of human ACE has been used to study different aspects of ACE biology. In this study we characterized the monoclonal **antibody** (mAb) 5F1, developed against the N domain of human ACE, which recognizes both the catalytically active and the denatured forms of ACE. The epitope for mAb 5F1 was defined using species cross-reactivity, synthetic peptide (PepScan technology) and phage display library **screening**, Western blotting, site-directed mutagenesis, and protein modeling. The epitope for mAb 5F1 shows no overlap with the epitopes of seven other mAbs to the N domain described previously and is localized on the other side of the N domain globule. The binding of mAb 5F1 to ACE is **carbohydrate-dependent** and increased significantly as a result of altered glycosylation after treatment with alpha-glucosidase-1 inhibitor, N-butyldeoxynojirimycin (NB-DNJ), or neuraminidase. Out of 17 species tested, mAb 5F1 showed strict primate ACE specificity. In addition, mAb 5F1 recognized human ACE in Western blots and on paraffin-embedded sections. The sequential part of the epitope for mAb 5F1 is created by the N-terminal part of the N domain, between residues 1 and 141. A conformational region of the epitope was also identified, including the residues around the glycan attached to Asn117, which explains the sensitivity to changes in glycosylation state, and another stretch localized around the motif 454TPPSRYN460. Site-directed mutagensis and inhibition assays revealed that mAb 5F1 inhibits ACE activity at high concentrations due to binding of residues on both sides of the active site cleft, thus supporting a hinge-bending mechanism for substrate binding of ACE.

L17 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 3

2003351603. PubMed ID: 12695908. Immunodiagnostically applicable monoclonal **antibodies** to the circulating anodic antigen of Schistosoma mansoni bind to small, defined oligosaccharide epitopes. Vermeer H J; van Dam G J; Halkes K M; Kamerling J P; Vliegenthart J F G; Hokke C H; Deelder A M. (Department of Parasitology, Center of Infectious Diseases, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands.) Parasitology research, (2003 Jul) Vol. 90, No. 4, pp. 330-6. Electronic Publication: 2003-04-15. Journal code: 8703571. ISSN: 0932-0113. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB Gut-associated glycoproteins constitute a major group of the circulating excretory antigens produced by human Schistosoma species. The O-glycans of the relatively abundant circulating anodic antigen (CAA) from S. mansoni carry long stretches of unique -->6(GlcA beta 1-->3)GalNAc beta

1--> repeats. Specific anti-carbohydrate monoclonal **antibodies** (mAbs) are essential tools for the immunodiagnostic detection of CAA in the serum or urine of Schistosoma-infected subjects. In order to define the epitopes recognised by these anti-CAA mAbs, we **screened** a series of protein-coupled synthetic di- to pentasaccharide building blocks of the CAA polysaccharide for immunoreactivity, using ELISA and surface plasmon resonance spectroscopy. It was shown that anti-CAA IgM mAbs preferentially recognise -->6(GlcA beta 1-->3)GalNAc beta 1--> disaccharide units. Interestingly, no mouse anti-CAA mAbs of the IgG class were found that bind to the synthetic epitopes, although many of the IgG mAbs tested do recognise native CAA in a **carbohydrate-dependent** manner. In addition, both IgM and IgG class **antibodies** could be detected in human infection sera using the synthetic CAA fragments. These synthetic schistosome glycan epitopes and their matching set of specific mAbs are useful tools that further the development of diagnostic methods and are helpful in defining the immunological responses of the mammalian hosts to schistosome glycoconjugates.

L17 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 4

2000129062. PubMed ID: 10667600. A peptide mimic of E-selectin ligand inhibits sialyl Lewis X-dependent lung colonization of tumor cells. Fukuda M N; Ohyama C; Lowitz K; Matsuo O; Pasqualini R; Ruoslahti E; Fukuda M. (The Burnham Institute, Cancer Research Center, La Jolla, California 92037, USA.. michiko@burnham-inst.org) . Cancer research, (2000 Jan 15) Vol. 60, No. 2, pp. 450-6. Journal code: 2984705R. ISSN: 0008-5472. Pub. country: United States. Language: English.

AB Selectins bind to carbohydrate ligands in a calcium-dependent manner and play critical roles in host defense and possibly in tumor metastasis. To isolate peptides that mimic E-selectin ligands, we **screened** a phage peptide library using E-selectin as a target molecule. This attempt unexpectedly failed, probably because the binding affinity of E-selectin to its ligand is low. We then took an approach that is analogous to the isolation of anti-idiotype **antibodies** and were able to isolate peptides that bound to anticarbohydrate **antibodies** recognizing E-selectin ligands. These peptides, enriched for their binding to anti-Lewis A **antibody**, were found to bind to E-, P- and L-selectins in a calcium-dependent manner. Phage harboring the identified peptide IELLQAR and synthetic peptides having the same sequence inhibited the binding of sialyl Lewis X or sialyl Lewis A oligosaccharides to E-selectin. The adhesion of HL-60 and B16 melanoma cells expressing sialyl Lewis X to E-selectin was also inhibited by the phage-displaying IELLQAR peptide. Moreover, i.v. injected IELLQAR peptide inhibited the lung colonization of mouse B16 melanoma and human lung tumor cells expressing sialyl Lewis X. These results demonstrate that it is possible to isolate peptides mimicking carbohydrate ligands by **screening** the peptides for binding to anticarbohydrate **antibodies** and then using them to inhibit **carbohydrate-dependent** experimental tumor metastasis.

L17 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 5

1991153563. PubMed ID: 1705525. **Carbohydrate-dependent** epitope mapping of human thyrotropin. Papandreou M J; Sergi I; Benkirane M; Ronin C. (Laboratoire de Biochemie, URA 1179 CNRS, Faculte de Medecine-Secteur Nord, Marseilles, France.) Molecular and cellular endocrinology, (1990 Oct 1) Vol. 73, No. 1, pp. 15-26. Journal code: 7500844. ISSN: 0303-7207. Pub. country: Netherlands. Language: English.

AB To probe possible effects of carbohydrate chains in the conformation of pituitary glycoprotein hormones, two radiolabeled derivatives of human thyroid-stimulating hormone (hTSH), either partially deglycosylated in the beta-subunit or fully deglycosylated in both the alpha- and beta-subunits, were compared to the native hormone for binding to monoclonal as well as

polyclonal **antibodies**. Monoclonal **antibodies** were **screened** for their ability to bind the intact hormone (anti-hTSH), hTSH and its free alpha-subunit (anti-alpha) or its free beta-subunit (anti-beta). A panel of 14 monoclonal **antibodies** directed against at least eight out of the 12 epitopes known to be present in the hormone was tested in solid-phase assays for their capacity to bind intact and deglycosylated forms of hTSH. All of them displayed identical recognition of native and partially deglycosylated 125I-hTSH. In contrast, binding of fully deglycosylated 125I-hTSH to anti-hTSH and anti-beta **antibodies** was dramatically lost while that of anti-alpha was preserved. This clearly indicates that most of the epitopes specific for subunit association as well as those present on the beta-subunit are glycosylation dependent. No alteration was found in **antibody** recognition following deglycosylation of free individual subunits, indicating that the carbohydrate effect can only occur in the combined dimer. Using polyclonal antisera raised against the International Reference Preparations, we found that the deglycosylated hormone could be bound by the anti-beta antiserum although at a much lower dilution than the native antigen, suggesting the presence of at least one glycosylation-independent epitope in the beta-subunit. Competitive binding assays revealed that deglycosylated hTSH is 5 times less immunoreactive toward the anti-beta compared to the anti-alpha antiserum. The current data thus demonstrate the presence of the glycosylation-independent epitopes in the alpha-subunit of hTSH and the localization of most of the glycosylation-dependent domains in the beta-subunit.

```
=> s recombinant human TSH
L18       1145 RECOMBINANT HUMAN TSH

=> s l18 and oversialylated
L19          0 L18 AND OVERSIALYLATED

=> s l18 and asialo recTSH
L20          0 L18 AND ASIALO RECTSH

=> s l18 and sialyation
L21          0 L18 AND SIALYATION

=> s recombinant human thyrotropin
L22        800 RECOMBINANT HUMAN THYROTROPIN

=> s l22 and oversialylated
L23          0 L22 AND OVERSIALYLATED

=> s l22 and sialylation
L24         20 L22 AND SIALYLATION

=> s l24 and branched
L25          0 L24 AND BRANCHED

=> s l24 and lectin chromatography
L26          0 L24 AND LECTIN CHROMATOGRAPHY

=> s l24 and fucosylation
L27          4 L24 AND FUCOSYLATION

=> dup remove l27
PROCESSING COMPLETED FOR L27
L28           2 DUP REMOVE L27 (2 DUPLICATES REMOVED)
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=> d l28 1-2 cbib abs

L28 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
2006028258. PubMed ID: 16372382. Characterization of N-glycans of **recombinant human thyrotropin** using mass spectrometry. Morelle Willy; Donadio Sandrine; Ronin Catherine; Michalski Jean-Claude. (Unite Mixte de Recherche CNRS/USTL 8576, Glycobiologie Structurale et Fonctionnelle, IFR 118, Universite des Sciences et Technologies de Lille 1, 59655 Villeneuve d'Ascq Cedex, France.. willy.morelle@univ-lille1.fr) . Rapid communications in mass spectrometry : RCM, (2006) Vol. 20, No. 3, pp. 331-45. Journal code: 8802365. ISSN: 0951-4198. Pub. country: England: United Kingdom. Language: English.

AB Thyroid-stimulating hormone is a vital component of the regulatory mechanism that maintains the structure and function of the thyroid gland and governs thyroid hormone release. In this paper we report the first detailed structural characterization of the N-linked oligosaccharides of recombinant human thyroid-stimulating hormone (rhTSH). Using a strategy combining mass spectrometric analysis and sequential exoglycosidase digestion, we have defined the structures of the N-glycans released from **recombinant human thyrotropin** by peptide N-glycosidase F. All glycans are complex-type glycans and are mainly of the bi- and triantennary type with variable degrees of **fucosylation** and **sialylation**. The major non-reducing epitope in the complex-type glycans is: NeuAcalpha2-3Galbeta1-4GlcNAc (sialylated LacNAc). The carbohydrate microheterogeneity at the three glycosylation sites was studied using reversed-phase high-performance liquid chromatography (RP-HPLC), concanavalin A affinity chromatography and mass spectrometric techniques, including both matrix-assisted laser desorption/ionization (MALDI) and electrospray. rhTSH was reduced, carboxymethylated and then digested with trypsin. The mixture of peptides and glycopeptides was subjected to RP-HPLC and the structures of the glycopeptides were determined by MALDI in conjunction with on-target exoglycosidase digestions. After PNGase F digestion, the peptide moiety of the glycopeptide was determined by the presence of the b- and y-series ions derived from its amino acid sequence in the quadrupole time-of-flight tandem mass (QTOF-MS/MS) spectrum. Glycosylation sites Asn-alpha52 and Asn-alpha78 contain mainly bi- and triantennary complex-type glycans. Only glycosylation site Asn-alpha52 bears fucosylated N-glycans. Minor tetraantennary complex structures were also observed on both glycosylation sites. Profiling of the carbohydrate moieties of Asn-beta23 indicates a large heterogeneity. Bi-, tri-, and tetraantennary N-glycans were present at this site. These data demonstrate site-specificity of glycosylation in the alpha subunit but not in the beta subunit of rhTSH with Asn-alpha52 bearing essentially di- and triantennary glycans with or without core **fucosylation** and bi- and triantennary glycans with no core **fucosylation** being attached to Asn-alpha78.

L28 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
2006:153674 Document No. 144:382215 Characterization of N-glycans of **recombinant human thyrotropin** using mass spectrometry. Morelle, Willy; Donadio, Sandrine; Ronin, Catherine; Michalski, Jean-Claude (Unite Mixte de Recherche CNRS/USTL 8576, "Glycobiologie Structurale et Fonctionnelle", Universite des Sciences et Technologies de Lille 1, Villeneuve d'Ascq, 59655, Fr.). Rapid Communications in Mass Spectrometry, Volume Date 2006, 20(3), 331-345 (English) 2005. CODEN: RCMSEF. ISSN: 0951-4198. Publisher: John Wiley & Sons Ltd..

AB TSH is a vital component of the regulatory mechanism that maintains the structure and function of the thyroid gland and governs thyroid hormone release. In this paper the authors report the first detailed structural characterization of the N-linked oligosaccharides of recombinant human TSH

(rhTSH). Using a strategy combining mass spectrometric anal. and sequential exoglycosidase digestion, the authors have defined the structures of the N-glycans released from recombinant human TSH by peptide N-glycosidase F. All glycans are complex-type glycans and are mainly of the bi- and triantennary type with variable degrees of **fucosylation** and **sialylation**. The major non-reducing epitope in the complex-type glycans is: NeuAcα2-3Galβ1-4GlcNAc (sialylated LacNAc). The carbohydrate microheterogeneity at the three glycosylation sites was studied using reversed-phase HPLC (RP-HPLC), Con A affinity chromatog. and mass spectrometric techniques, including both matrix-assisted laser desorption/ionization (MALDI) and electrospray. RhTSH was reduced, carboxymethylated and then digested with trypsin. The mixture of peptides and glycopeptides was subjected to RP-HPLC and the structures of the glycopeptides were determined by MALDI in conjunction with on-target exoglycosidase digestions. After PNGase F digestion, the peptide moiety of the glycopeptide was determined by the presence of the b- and y-series ions derived from its amino acid sequence in the quadrupole time-of-flight tandem mass (QTOF-MS/MS) spectrum. Glycosylation sites Asn-α52 and Asn-α78 contain mainly bi-and triantennary complex-type glycans. Only glycosylation site Asn-α52 bears fucosylated N-glycans. Minor tetraantennary complex structures were also observed on both glycosylation sites. Profiling of the carbohydrate moieties of Asn-β23 indicates a large heterogeneity. Bi-, tri-, and tetraantennary N-glycans were present at this site. These data demonstrate site-specificity of glycosylation in the α subunit but not in the β subunit of rhTSH with Asn-α52 bearing essentially di- and triantennary glycans with or without core **fucosylation** and bi- and triantennary glycans with no core **fucosylation** being attached to Asn-α78.

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=> s l22 and antibod?
L29        152 L22 AND ANTIBOD?

=> s l29 and screen?
L30          6 L29 AND SCREEN?

=> dup remove l30
PROCESSING COMPLETED FOR L30
L31           4 DUP REMOVE L30 (2 DUPLICATES REMOVED)

=> d l31 1-4 cbib abs

L31  ANSWER 1 OF 4     MEDLINE on STN
2006218519.    PubMed ID: 16624113.   The relationship between serum thyroid
     autoantibodies, iodine intake, development and prognosis of Graves'
     disease. Chen Wei; Man Na; Li Yu-shu; Shan Zhong-yan; Teng Wei-ping.
     (Endocrinology Department, Endocrinology Institute, The First Affiliated
     Hospital of China Medical University, Shenyang 110001, China. ) Zhonghua
     nei ke za zhi [Chinese journal of internal medicine], (2006 Feb) Vol. 45,
     No. 2, pp. 95-9.  Journal code: 16210490R. ISSN: 0578-1426. Pub. country:
     China. Language: Chinese.
AB   OBJECTIVE: To investigate the relationship of thyroid autoantibodies
     including serum thyroid stimulating antibody (TSAb), thyroid
     stimulation blocking antibody (TSBAb) and iodine intake with the
     development and prognosis of Graves' hyperthyroidism.  METHODS: A total of
     63 subjects with overt hyperthyroidism were screened out from 3
     Chinese rural communities with different iodine intakes at first survey.
     Serum TSAb, TSBAb, thyrotropin binding inhibitory immunoglobulin (TBII),
     thyroid peroxidase antibody (TPOAb) and thyroglobulin
     antibody (TGAb) were detected.  The patients were followed up 2
     years later.  TSAb and TSBAb were measured with recombinant
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human thyrotropin receptor (rhTSHR)-Chinese hamster ovary cell (rhTSHR-CHO cell) bioassay. RESULTS: At the first survey, the prevalences of positive TSAb, TBII and TSBAb were found in 80.9%, 61.7% and 6.4% of the patients with Graves' disease respectively. TSAb and/or TBII were positive in 91.5% of the patients. The consistent rate of TSAb and TBII was 59.6% in the cases. All indexes mentioned above were higher in the patients than in healthy controls. Positive correlations were found between TSAb and TBII (r = 0.407), TSAb and thyroglobulin (r = 0.301), TSAb and thyroid volume (r = 0.317) respectively. The prevalence of positive TSAb (91.7%) in Graves' patients in iodine excessive area are significantly higher than those in iodine mildly deficient area (66.7%). The positive rates and the titers of TBII, TPOAb and TGAb were not different statistically among the patients in the three communities. At follow-up, the patients with Graves' hyperthyroidism were classified into euthyroid group (G1) and hyperthyroid group (G2) according to their outcomes of the disease. The TSAb titers and the thyroid volume in the cases of G1 decreased significantly, whereas the patients with highly positive TPOAb titers in the first survey and the follow-up were hard to become euthyroid and TSAb may be the secondary factor influencing the thyroid as compared with TPOAb. CONCLUSION: TSAb is more significant than TBII in diagnosing and predicting the outcomes of Graves' hyperthyroidism. The application of both TSAb and TBII could raise the positive rates of thyrotrophin receptor **antibody** tests. TSAb, TPOAb titers and thyroid volume were factors influencing the prognosis of Graves' hyperthyroidism.

L31 ANSWER 2 OF 4 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

2004:38440 The Genuine Article (R) Number: 756YR. Three-week thyroxine withdrawal thyroglobulin stimulation **screening** test to detect low-risk residual/recurrent well-differentiated thyroid carcinoma.

Walfish P G (Reprint). Mt Sinai Hosp, Endocrine Unit, Rm 782, 600 Univ Ave, Toronto, ON M5G 1X5, Canada (Reprint). Golger A; Fridman T R; Eski S; Witterick I J; Freeman J L. Mt Sinai Hosp, Dept Otolaryngol, Toronto, ON, Canada; Mt Sinai Hosp, Dept Med, Toronto, ON, Canada; Univ Toronto, Med Sch, Toronto, ON, Canada.

JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION (OCT 2003) Vol. 26, No. 10, pp. 1023-1031. ISSN: 0391-4097. Publisher: EDITRICE KURTIS S R L, VIA LUIGI ZOJA 30, 20153 MILAN, ITALY. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Measurement of serum TSH-stimulated thyroglobulin (Tg) is recognized as a sensitive method for detecting residual/recurrent well-differentiated thyroid carcinoma (WDTC) in patients previously treated by surgery and radioactive iodine (RAI) ablation therapy. WDTC patients who have an undetectable serum Tg on thyroid hormone therapy (THT) in the absence of Tg-**antibody** interference are considered to be at low risk for residual/recurrent disease. Traditional management has been to withdraw T-4 for 4-6 weeks or T-3 for 2 weeks to stimulate endogenous TSH. However, this prolonged THT withdrawal induces hypothyroidism and its concomitant morbidity. In the present study, we assess the efficacy of shortening the time of T-4 withdrawal to only 3 weeks for detecting residual/recurrent WDTC as a sufficient serum TSH stimulus for obtaining a positive serum Tg result without a routine diagnostic whole body scan (WBS). Additionally, we have evaluated the impact of such a T-4 withdrawal interval on quality of life and loss of employment time. A total of 181 patients with WDTC selected for study had previously been treated with a bilateral surgical thyroidectomy followed by RAI ablation therapy (average post-surgery to follow-up interval of 10.8 yr). All of the cohort had an undetectable (<1 mug/l) serum Tg on THT without Tg-**antibody** interference. Serum TSH and Tg were measured before and after cessation of T-4 therapy for 3 weeks. A serum Tg greater than or equal to2 mug/l was considered positive for residual/recurrent disease. A

quality of life questionnaire [Short-Form 36 (SF-36)] was administered before withdrawal, at peak TSH and after resumption of therapy. From the completed SF-36 questionnaires, the overall degree of functional impairment was not severe and did not result in loss of employment time. Moreover, this protocol identified three possible responses to the 3-week T-4 withdrawal interval as follows: a) serum Tg undetectable with TSH 25 mIU/l (similar to75% of total cohort); b) serum Tg greater than or equal to2 mug/l (similar to10% of total cohort) which will require further investigation and treatment for residual/recurrent disease; c) undetectable serum Tg with inadequate TSH rise (similar to15% of total cohort), which will require TSH stimulation by either longer T-4 withdrawal or recombinant human TSH to exclude residual disease. We conclude that a stimulated serum Tg test performed 3 weeks after T-4 withdrawal is a simple and cost-effective first-line **screening** test with minimal morbidity which is sufficient to evaluate low-risk WDTC patients for recurrent/residual carcinoma. (C) 2003, Editrice Kurtis.

L31 ANSWER 3 OF 4 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

2002270409 EMBASE Management of low-risk well-differentiated thyroid cancer based only on thyroglobulin measurement after **recombinant human thyrotropin.**

Wartofsky, Leonard, Dr. (correspondence). Department of Medicine, Washington Hospital Center, 110 Irving Street, N.W., Washington, DC 20010-2975, United States. Leonard.wartofsky@medstar.net.

Thyroid Vol. 12, No. 7, pp. 583-590 2002.

Refs: 20.

ISSN: 1050-7256. CODEN: THYRER.

Pub. Country: United States. Language: English. Summary Language: English.

Entered STN: 20020815. Last Updated on STN: 20020815

AB A multicenter study was undertaken to ascertain prevalence and significance of **recombinant human thyrotropin** (rhTSH)-stimulated increases in thyroglobulin (Tg) levels in thyroid cancer patients classified to be at low risk for recurrence. Patients were eligible for enrollment if they had undergone near-total or total thyroidectomy and remnant ablation between 1-10 years prior to enrollment and had received thyroxine suppression therapy (THST) with a TSH level of < 0.5 mU/L and Tg level less than or equal to 5 ng/mL within the prior year. Patients with anti-Tg **antibodies**, distant metastases, or other evidence of residual disease were excluded. Four hundred eighty-six patients were entered into the study, and 300 were considered eligible and comprise the study population. TSH, Tg, and anti-Tg **antibody** levels were obtained at baseline, followed by intramuscular injection of 0.9 mg of rhTSH on days 1 and 2 and measurement of Tg on day 5. After rhTSH, 53 patients (18%) had elevations in Tg of at least 2 ng/mL, including 33 patients (11%) with increases from baseline of equal to or greater than 5 ng/mL. Patients with an initial advanced stage of disease were more likely to display elevations in Tg after rhTSH. One third of those with stage III disease displayed elevations in Tg of 2 ng/mL or more. Patients within 5 years of thyroidectomy were as likely to display elevations in rhTSH-stimulated Tg as those 5-10 years from surgery. In conclusion, these data suggest rhTSH-stimulated Tg testing without scan may be a useful tool in the follow-up of patients with low-risk thyroid cancer, and may serve to identify patients previously thought free of disease on the basis of undetectable Tg levels while undergoing THST. A strategy is presented for incorporation of this approach into the management of patients with low-risk well-differentiated thyroid cancer.

L31 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 1

1998241859. PubMed ID: 9580758. Bioassay of thyrotropin receptor **antibodies** with Chinese hamster ovary cells transfected with **recombinant human thyrotropin** receptor:

clinical utility in children and adolescents with Graves disease. Botero D; Brown R S. (Department of Pediatrics, University of Massachusetts Medical School, Worcester, USA.) The Journal of pediatrics, (1998 Apr) Vol. 132, No. 4, pp. 612-8. Journal code: 0375410. ISSN: 0022-3476. Pub. country: United States. Language: English.

AB OBJECTIVE: The objective of this study was to compare the clinical utility of a new bioassay for thyrotropin (TSH) receptor **antibodies** (Abs) with the conventional radioreceptor assay and with measurement of thyroid peroxidase Abs in the diagnosis of Graves disease in childhood. STUDY DESIGN: Serum samples obtained from 22 children and adolescents with Graves disease (19 hyperthyroid, 3 in remission), 13 children and adolescents with chronic lymphocytic thyroiditis, and 17 normal children in a control group were evaluated. RESULTS: TSH receptor Abs were detected by bioassay in 10 (91%) of 11 patients with active Graves disease but in 0 of 2 patients in remission, 0 of 13 normal members of the control group, and 0 of 11 patients with chronic lymphocytic thyroiditis including 1 with thyrotoxicosis. The sensitivity and specificity of TSH receptor Abs detected by radioreceptor assay studied in the same 11 patients and in an additional 11 patients was similar to bioassay. In contrast, thyroid peroxidase Abs were detected in only 12 (71%) of 17 patients with Graves disease but in 11 of 11 patients with chronic lymphocytic thyroiditis and in 0 of 17 members of the control group. CONCLUSION: Bioassay of TSH receptor Abs is both sensitive and specific for the diagnosis of active Graves disease in the young. When cost and simplicity are considered, however, bioassay offers no advantage over radioreceptor assay for initial diagnostic **screening**. Rather, bioassay for TSH receptor Abs may be useful in thyrotoxic patients who are negative initially in the radioreceptor assay or in treated patients whose clinical picture is discordant with results in the radioreceptor assay.

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=> s l22 and lentil chromatography
L32          0 L22 AND LENTIL CHROMATOGRAPHY

=> s l22 and chromatography
L33         24 L22 AND CHROMATOGRAPHY

=> s l33 and conA
L34          0 L33 AND CONA

=> s l33 and lentil
L35          0 L33 AND LENTIL

=> s l33 and desialylated
L36          0 L33 AND DESIALYLATED

=> dup remove l33
PROCESSING COMPLETED FOR L33
L37          10 DUP REMOVE L33 (14 DUPLICATES REMOVED)

=> s l37 and pd<20040204
   1 FILES SEARCHED...
   4 FILES SEARCHED...
L38          5 L37 AND PD<20040204

=> dup remove l38
PROCESSING COMPLETED FOR L38
L39           5 DUP REMOVE L38 (0 DUPLICATES REMOVED)

=> d l39 1-5 cbib abs

L39  ANSWER 1 OF 5     MEDLINE on STN
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1999299935. PubMed ID: 10372720. Analysis of carbohydrate residues on **recombinant human thyrotropin** receptor. Oda Y; Sanders J; Roberts S; Maruyama M; Kiddie A; Furmaniak J; Smith B R. (FIRS Laboratories, RSR Ltd., Llanishen, Cardiff, United Kingdom.) The Journal of clinical endocrinology and metabolism, **(1999 Jun)** Vol. 84, No. 6, pp. 2119-25. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB An investigation of the sugar groups on recombinant human TSH receptors (TSHR) expressed in CHO-K1 cells and solubilized with detergents is described. Western blotting studies with TSHR monoclonal antibodies showed that the receptor was present principally as two bands with approximate molecular masses of 120 and 100 kDa. Further blotting studies using lectins and/or involving treatment with different glycosidases indicated that the 100-kDa band contained about 16 kDa of high mannose-type sugars, and the 120-kDa band contained about 33 kDa of complex-type sugars. It was possible to separate the 120- and 100-kDa components of the TSHRs by lectin affinity **chromatography**. In particular, Galanthus nivalis lectin, which binds high mannose-type sugars, bound the 100-kDa band, but not the 120-kDa band, whereas Datura stramonium lectin, which binds complex-type sugars, bound the 120-kDa band, but not the 100-kDa band. 125I-Labeled TSH binding studies with the various lectin column fractions showed that TSH-binding activity was principally associated with the complex-type sugar containing the 120-kDa form of the receptor rather than the high mannose-containing 100-kDa form. During peptide chain glycosylation, high mannose-type sugar residues are attached first and then modified by the formation of complex type structures to form the mature glycoprotein. Our data suggest that in the case of the TSH receptor, this type of posttranslational processing has an important role in forming the TSH-binding site.

L39 ANSWER 2 OF 5 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

1998:689498 The Genuine Article (R) Number: 117GC. Modulation of human thyrotropin oligosaccharide structures - enhanced proportion of sialylated and terminally galactosylated serum thyrotropin isoforms in subclinical and overt primary hypothyroidism.
Schaaf L (Reprint). Max Planck Inst Psychiat, Kraepelinstr 10, D-80804 Munchen, Germany (Reprint). Trojan J; Theodoropoulou M; Usadel K H; Stalla G K. Max Planck Inst Psychiat Endokrinol & Klin Chem, D-80804 Munchen, Germany; Univ Frankfurt Klinikum, Zentrum Inneren Med, D-60590 Frankfurt, Germany.
JOURNAL OF ENDOCRINOLOGY (**SEP 1998**) Vol. 158, No. 3, pp. 359-365. ISSN: 0022-0795. Publisher: SOC ENDOCRINOLOGY, 17/18 THE COURTYARD, WOODLANDS, BRADLEY STOKE, BRISTOL BS32 4NQ, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Enhanced sialylation of thyrotropin (TSH) prolongs its metabolic clearance rate and thus increases the hormone's in vivo bioactivity. This has been shown for hypothyroid rats and for recombinant human TSH, but there are few data on the sialylation of human serum TSH. The aim of this work was to further study sialylated human serum TSH, its precursors bearing terminal galactose residues, and the role of pharmacological doses of thyrotropin-releasing hormone (TRH) on their secretion under different degrees of primary hypothyroidism.

We analyzed serum TSH in patients with subclinical (n=9) and overt primary hypothyroidism (n=13) compared with euthyroid individuals (n=12) and human standard pituitary TSH (IRP 80/558). Blood was drawn before and 30 min after intravenous administration of 200 mu g TRH, and TSH was purified by immunoaffinity concentration. The content of sialylated (sialo-) TSH and isoforms bearing terminal galactose (Gal-TSH, asialo-Gal-TSH) was measured by Ricinus communis (RCA 120) affinity **chromatography** in combination with enzymatic cleavage of sialic

acid residues. TSH immunoreactivity was measured by an automated second generation TSH immunoassay.

Pituitary TSH contained 16.5 +/- 0.8% Gal-TSH. In euthyroid individuals the proportion of Gal-TSH was 14.6 +/- 9%, whereas TSH in patients with subclinical and overt primary hypothyroidism contained 23.9 +/- 3.5% (P<0.05 vs euthyroid individuals) and 21.1 +/- 1.7% Gal-TSH respectively. The mean ratio of asialo-Gal TSH was 23.8 +/- 0.6% for pituitary TSH, 35.7 +/- 4.2% in euthyroid individuals, 48.0 +/- 3.3% in patients with subclinical, and 61.5 +/- 3.8% (P<0.001 vs euthyroid individuals) in patients with overt primary hypothyroidism. For pituitary TSH the calculated proportion of sialo-TSH was 65 +/- 0.2%, for euthyroid individuals 20.3 +/- 2.8%, for patients with subclinical hypothyroidism 24.1 +/- 3.0%, and for patients with overt primary hypothyroidism 40.7 +/- 3.0% (P<0.001 vs euthyroid individuals). The proportions of Gal-TSH, asialo-Gal-TSH, and sialo-TSH did not differ significantly before and after TRH administration in the individuals studied.

Our data show that patients with subclinical and overt primary hypothyroidism have a markedly increased proportion of serum TSH isoforms bearing terminal galactose and sialic acid residues, which may represent a mechanism for the further stimulation of thyroid function. Pharmacological doses of TRH cause an increased quantity of TSH to be released, but do not significantly alter the proportion of sialylated or terminally galactosylated TSH isoforms.

L39 ANSWER 3 OF 5 MEDLINE on STN

1996368590. PubMed ID: 8772598. Large scale synthesis of **recombinant human thyrotropin** using methotrexate amplification: chromatographic, immunological, and biological characterization. Hussain A; Zimmerman C A; Boose J A; Froehlich J; Richardson A; Horowitz R S; Collins M T; Lash R W. (Department of Medicine, University of Maryland School of Medicine, Baltimore, USA.) The Journal of clinical endocrinology and metabolism, **(1996 Mar)** Vol. 81, No. 3, pp. 1184-8. Journal code: 0375362. ISSN: 0021-972X. Pub. country: United States. Language: English.

AB Studies of human TSH (hTSH) structure and function have been limited by difficulties in producing large quantities of recombinant hormone. We describe a system for the stable expression of high levels of recombinant human TSH (rec hTSH) using a mutant form of dihydrofolate reductase (dhfr) as an amplifiable dominant selectable marker. A vector expressing both the hTSH alpha-subunit and the mutant dhfr was cotransfected with a hTSH beta-subunit expression vector into dhfr-deficient cells. Amplification of the transfected sequences by methotrexate selection, followed by cell culture in a hollow fiber perfusion system, yielded rec hTSH production as high as 100,000 microU/ mL. Immunoradiometric assays using five different antibodies revealed no differences in the immunological activities of rec hTSH and pituitary hTSH. Bioactivity was measured in a novel TSH bioassay coupling the generation of cAMP by a transfected hTSH receptor to the cAMP-dependent regulation of a luciferase reporter gene. The ED50 for bovine TSH in this bioassay was 1.4 ng/mL (3.5 x 10(-11) mol/L). The ratio of the ED50 values for rec hTSH and pituitary hTSH was 1.0:1.1 (P = NS), indicating that the two TSHs were of equivalent potency. In conclusion, we have developed techniques for the high level production of rec hTSH that is immunologically and biologically equivalent to pituitary hTSH. The ability to produce large quantities of rec hTSH using standard laboratory techniques should facilitate future studies, such as the development of clinically useful TSH analogs.

L39 ANSWER 4 OF 5 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

1996:683559 The Genuine Article (R) Number: VH267. Glycosylation is the structural basis for changes in polymorphism and immunoreactivity of pituitary glycoprotein hormones.

Zerfaoui M (Reprint); Ronin C. UPR 9024 CNRS, GLM, F-13402 MARSEILLE 20, FRANCE.
EUROPEAN JOURNAL OF CLINICAL CHEMISTRY AND CLINICAL BIOCHEMISTRY (**SEP 1996**) Vol. 34, No. 9, pp. 749-753. ISSN: 0939-4974. Publisher: WALTER DE GRUYTER & CO, GENTHINER STRASSE 13, D-10785 BERLIN, GERMANY. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Glycoprotein hormones have long been known to display extensive polymorphism and changes in bioactivity according to the endocrine status of the patient. Structural analysis has shown that pituitary gonadotropins (lutropin and follitropin) and thyrotropin are synthesized and secreted as a panel of isoforms which differ in glycosylation, bioactivity and circulatory half-life. Ultrasensitive immunoassays could reveal that glycosylation of plasma hormones is structurally different from the pituitary stock so that the ratio of circulating glycoforms may vary according to the physiopathology of the pituitary axis. However, contradictory results between immunoassays have been often reported, suggesting that some plasma forms can escape recognition by monoclonal antibodies which have been raised to the pituitary or urinary antigen. When hormone levels do not correlate with clinical features, one can also suspect that inactive or hyperactive forms are being measured. At the molecular level, very limited information has been gained toward the expression of hormone epitopes as a function of carbohydrate structure. To adress this issue, we have compared the recognition of pituitary and **recombinant human thyrotropin** by various polyclonal and monoclonal antibodies before and after neuraminidase treatment. Both, pituitary and recombinant thyrotropin bound to anti-alpha and anti-beta antibodies, demonstrating thereby that recombinant thyrotropin can be used to calibrate immunoassays. While removal of sialic acid did not alter the recognition of the recombinant hormone in various immunoassays, this treatment specifically abolished the binding of pituitary thyrotropin to anti-beta monoclonal antibodies. These findings show that immunoreactivity of circulating hormone glycoforms, which are often more sialylated thant their pituitary counterparts, may very well account for variation depending on the antibodies used in the immunoassays.

L39 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
1996:48889 Document No. 124:76675 Original Reference No. 124:14060h,14061a
The use of **recombinant human thyrotropin** produced by Chinese Hamster Ovary cells for the preparation of immunoassay reagents. Ribela, Maria Teresa C. P.; Bianco, Antonio C.; Bartolini, Paolo (Department of Application of Nuclear Techniques in Biological Sciences, National Nuclear Energy Commission, Sao Paulo, Brazil). Journal of Clinical Endocrinology and Metabolism, 81(1), 249-56 (English) **1996**. CODEN: JCEMAZ. ISSN: 0021-972X. Publisher: Endocrine Society.

AB Recombinant human TSH (rec-hTSH; Thyrogen, lot M-17073) obtained from transformed Chinese hamster ovary cells was tested for both radioiodination and preparation of a secondary standard used in RIA and immunoradiometric assay (IRMA) for routine clin. investigation. Results were compared to those obtained with high quality pituitary TSH (pit-hTSH; Dr. P. Torjesen, Oslo, Norway; and NIDDK, Rockville MD), traditionally used in these assays. After extensive characterization and testing, it was found that [125I]rec-hTSH matched all binding and **chromatog.** critical usually obtained with [125I]pit-hTSH, including Stokes' radius, labeling, and storage stability, and did not introduce any significant bias when used in the measurement of unknown serum samples. A preparation of rec-hTSH was calibrated against a local secondary standard as well as against two well known international reference prepns. (NIDDK hTSH RP-1 and WHO International Reference Preparation 80/558) by IRMA and RIA. In the RIA, NIDDK anti-hTSH-3 polyclonal antibody was used, whereas in the IRMA, two com.

prepns. were used: a monoclonal antibody as the capture antibody. In both assays, the recombinant standard preparation yielded good fit displacement curves, showing significant parallelism compared to pit-hTSH and therefore allowing an unbiased measurement of unknown serum samples. The specific activity of the rec-hTSH preparation calibrated against the WHO International Reference Preparation was 7.7 IU/mg protein when measured by IRMA and 71 IU/mg when measured by RIA. In conclusion, these results indicate for the first time that rec-hTSH can fully replace pit-hTSH as both standard and tracer in diagnostic in vitro systems such as RIA and IRMA, suggesting that other recombinant glycosylated hormones might also serve for immunoassay reagent preparation

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	186.51	186.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.92	-4.92

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LOGINID:SSSPTA1644PNH

PASSWORD:
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NEWS	2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS	3	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS	4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS	5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents

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 NEWS  6  SEP 09  50 Millionth Unique Chemical Substance Recorded in
                  CAS REGISTRY
 NEWS  7  SEP 11  WPIDS, WPINDEX, and WPIX now include Japanese FTERM
                  thesaurus
 NEWS  8  OCT 21  Derwent World Patents Index Coverage of Indian and
                  Taiwanese Content Expanded
 NEWS  9  OCT 21  Derwent World Patents Index enhanced with human
                  translated claims for Chinese Applications and
                  Utility Models
 NEWS 10  NOV 23  Addition of SCAN format to selected STN databases
 NEWS 11  NOV 23  Annual Reload of IFI Databases
 NEWS 12  DEC 01  FRFULL Content and Search Enhancements
 NEWS 13  DEC 01  DGENE, USGENE, and PCTGEN: new percent identity
                  feature for sorting BLAST answer sets
 NEWS 14  DEC 02  Derwent World Patent Index: Japanese FI-TERM
                  thesaurus added
 NEWS 15  DEC 02  PCTGEN enhanced with patent family and legal status
                  display data from INPADOCDB
 NEWS 16  DEC 02  USGENE: Enhanced coverage of bibliographic and
                  sequence information
 NEWS 17  DEC 21  New Indicator Identifies Multiple Basic Patent
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=> s screening
L1 1310026 SCREENING

=> s l1 and glycoform specific antibod?
L2 1 L1 AND GLYCOFORM SPECIFIC ANTIBOD?

=> d l2 cbib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN
2005:823920 Document No. 143:244656 Process for **screening glycoform-specific antibodies**. Ronin, Catherine; Donadio, Sandrine (Centre National de la Recherche Scientifique, Fr.; Universite de Provence Aix-Marseille 1). PCT Int. Appl. WO 2005076013 A2 20050818, 83 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-EP1160 20050204. PRIORITY: EP 2004-290290 20040204.
AB The present invention relates to the use of the assessment of the binding between - antibodies elicited against a first glycoprotein, and - at least one glycoform of a second glycoprotein, said second glycoprotein being itself a glycoform of the first protein, wherein said glycoform of the second glycoprotein is selected from a group of glycoforms of the second glycoprotein, each glycoform of said group corresponding to a determined glycosylation state defined by a determined sialylation state, and/or a determined branching state, and/or a determined fucosylation state, provided that said glycosylation state is not uniquely defined by a substantially unsialylated state, for the **screening** of **glycoform specific antibodies** directed against a given glycoform of the second glycoprotein.

=> s l1 and antibod?
L3 111274 L1 AND ANTIBOD?

=> s l3 and recombinant human TSH
L4 10 L3 AND RECOMBINANT HUMAN TSH

=> s l4 and glycosylation
L5 0 L4 AND GLYCOSYLATION

=> dup remove l4
PROCESSING COMPLETED FOR L4
L6 3 DUP REMOVE L4 (7 DUPLICATES REMOVED)

=> d l6 1-3 cbib abs

L6 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
2005318651. PubMed ID: 15967085. Papillary thyroid cancer: medical management and follow-up. Kloos Richard T. (The Ohio State University, 446 McCampbell Hall, 1581 Dodd Drive, Columbus, OH 43210-1296, USA.. Kloos-1@medctr.osu.edu) . Current treatment options in oncology, (2005 Jul) Vol. 6, No. 4, pp. 323-38. Ref: 111. Journal code: 100900946. ISSN:

1527-2729. Pub. country: United States. Language: English.

AB The incidence of epithelial derived thyroid cancer (papillary thyroid cancer and follicular thyroid cancer, known collectively as differentiated thyroid cancer) is rising. About 80% of patients with thyroid cancer have PTC and are best treated with thyroidectomy and functional lymph node dissection, followed by radioiodine ablation or therapy and performance of a posttreatment whole-body scan, followed by thyroid stimulating hormone (TSH) suppression. One year after radioiodine administration, the use of sensitive thyroglobulin (Tg) assays can separate the vast majority of patients with persistent disease from those who are free of disease and unlikely to have recurrent disease all without the need for repeat whole-body radioiodine imaging. Patients with detectable serum Tg during TSH suppression (Tg-on) or Tg that rises above 2 ng/mL after TSH stimulation (TSH-Tg) are highly likely to harbor residual tumor. TSH stimulation can be achieved using either thyroid hormone withdrawal or **recombinant human TSH** (rhTSH). Highly skilled **screening** neck ultrasonography can identify a few additional patients with subcentimeter residual neck lymph node metastases not detected by TSH-Tg. However, ultrasonography and chest computed tomography (CT) are most critical for tumor localization in those patients with Tg values that suggest residual disease or in those patients with persistent antithyroglobulin **antibodies** (TgAb) that falsely lower Tg measurement. TgAb quantitative titers typically resolve steadily over just a few years in patients free of disease after initial therapy. Another paradigm shift is the recognition that most patients who eventually achieve freedom from disease do so by surgery with fewer patients cured by repetitive radioiodine treatments, and even fewer cured with external beam radiation. Patients who appear to be free of disease require a lifetime of follow-up to optimize levothyroxine treatment, and they will undergo periodic stimulation testing because some will still manifest recurrent disease. Patients with persistent disease despite negative ultrasonography, chest CT, and whole-body radioiodine imaging may have a tumor identified by fluorodeoxyglucose positron emission tomography, optimally performed with combined TSH stimulation and image fusion with CT or magnetic resonance imaging. Patients with metastatic disease who are unresponsive to conventional treatment are encouraged to participate in increasingly available thyroid cancer-specific clinical trials using targeted experimental oral or intravenous chemotherapeutic agents to address this tumor that has historically proven resistant to conventional chemotherapeutic agents.

L6 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2

2004057864. PubMed ID: 14759077. Three-week thyroxine withdrawal thyroglobulin stimulation **screening** test to detect low-risk residual/recurrent well-differentiated thyroid carcinoma. Golger A; Fridman T R; Eski S; Witterick I J; Freeman J L; Walfish P G. (Department of Otolaryngology, Mount Sinai Hospital, University of Toronto Medical School, Toronto, Ontario, Canada.) Journal of endocrinological investigation, (2003 Oct) Vol. 26, No. 10, pp. 1023-31. Journal code: 7806594. ISSN: 0391-4097. Pub. country: Italy. Language: English.

AB Measurement of serum TSH-stimulated thyroglobulin (Tg) is recognized as a sensitive method for detecting residual/recurrent well-differentiated thyroid carcinoma (WDTC) in patients previously treated by surgery and radioactive iodine (RAI) ablation therapy. WDTC patients who have an undetectable serum Tg on thyroid hormone therapy (THT) in the absence of Tg-**antibody** interference are considered to be at low risk for residual/recurrent disease. Traditional management has been to withdraw T4 for 4-6 weeks or T3 for 2 weeks to stimulate endogenous TSH. However, this prolonged THT withdrawal induces hypothyroidism and its concomitant morbidity. In the present study, we assess the efficacy of shortening the time of T4 withdrawal to only 3 weeks for detecting residual/recurrent WDTC as a sufficient serum TSH stimulus for obtaining a positive serum Tg

result without a routine diagnostic whole body scan (WBS). Additionally, we have evaluated the impact of such a T4 withdrawal interval on quality of life and loss of employment time. A total of 181 patients with WDTC selected for study had previously been treated with a bilateral surgical thyroidectomy followed by RAI ablation therapy (average post-surgery to follow-up interval of 10.8 yr). All of the cohort had an undetectable (< 1 microg/l) serum Tg on THT without Tg-**antibody** interference. Serum TSH and Tg were measured before and after cessation of T4 therapy for 3 weeks. A serum Tg > or = 2 microg/l was considered positive for residual/recurrent disease. A quality of life questionnaire [Short-Form 36 (SF-36)] was administered before withdrawal, at peak TSH and after resumption of therapy. From the completed SF-36 questionnaires, the overall degree of functional impairment was not severe and did not result in loss of employment time. Moreover, this protocol identified three possible responses to the 3-week T4 withdrawal interval as follows: a) serum Tg undetectable with TSH > or = 25 mIU/l (approximately 75% of total cohort); b) serum Tg > or = 2 microg/l (approximately 10% of total cohort) which will require further investigation and treatment for residual/recurrent disease; c) undetectable serum Tg with inadequate TSH rise (approximately 15% of total cohort), which will require TSH stimulation by either longer T4 withdrawal or **recombinant human TSH** to exclude residual disease. We conclude that a stimulated serum Tg test performed 3 weeks after T4 withdrawal is a simple and cost-effective first-line **screening** test with minimal morbidity which is sufficient to evaluate low-risk WDTC patients for recurrent/residual carcinoma.

L6 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 3
1996407409. PubMed ID: 8811462. Epitope mapping of a **recombinant human TSH** receptor extracellular domain: identification of a predominant epitope using animal sera. Hunt N; Willey K P; Abend N; Northemann W; Leidenberger F A. (Institute for Hormone and Fertility Research, University of Hamburg, Germany.) Journal of clinical laboratory analysis, (1996) Vol. 10, No. 4, pp. 193-204. Journal code: 8801384. ISSN: 0887-8013. Pub. country: United States. Language: English.

AB The extracellular domain of the TSH receptor (TSHR-561, amino acids #78-389) was expressed as a hexa-histidine fusion protein in bacteria. The recombinant protein was purified to homogeneity and used to immunize porcine and ovine species. High titre **antibodies** were obtained from both species that recognized the recombinant protein in Western blot analysis but failed to interfere with the TSH radio receptor assay. An epitope library was constructed and screened with affinity purified ovine and porcine antisera and detected a number of positive clones. Sequence analysis revealed that all of the epitopes contained sequences derived from the carboxyl terminus of the recombinant immunogen. One clone defined an epitope covering 16 amino acids from the carboxyl terminus and was the common epitope found in all of the other clones. Western blot **screening** of a large panel of Graves' sera with recombinant TSH receptor protein identified one patient sera that also recognized linear epitopes in the TSHR-561 protein. Experimentation demonstrated that the linear epitope recognized by this human sera was identical to the sequence recognised by the animal antisera. This sequence is unique to the TSH receptor and will be useful in further studies to analyze the TSH receptor protein.

=> s l3 and high affinity
L7 1661 L3 AND HIGH AFFINITY

=> s l7 and rTSH
L8 0 L7 AND RTSH

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=> s l7 and TSH
L9          25 L7 AND TSH

=> s l9 and more branched
L10          0 L9 AND MORE BRANCHED

=> s l9 and recombinant
L11          2 L9 AND RECOMBINANT

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12           2 DUP REMOVE L11 (0 DUPLICATES REMOVED)

=> d l12 1-2 cbib abs

L12  ANSWER 1 OF 2  SCISEARCH  COPYRIGHT (c) 2009 The Thomson Corporation  on
     STN
1997:287396   The Genuine Article (R) Number: WT150. Insight into
     screening immunoglobulin gene combinatorial libraries in a phage
     display vector: A tale of two antibodies.
     Kakinuma A (Reprint); Portolano S; Chazenbalk G; Rapoport B; McLachlan S
     M. VET ADM MED CTR, THYROID MOL BIOL UNIT 111T, SAN FRANCISCO, CA 94121.
     AUTOIMMUNITY (1997) Vol. 25, No. 2, pp. 73-84. ISSN: 0891-6934. Publisher:
     HARWOOD ACAD PUBL GMBH, C/O STBS LTD, PO BOX 90, READING, BERKS, ENGLAND
     RG1 8JL. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB        Combinatorial libraries of immunoglobulin genes in ''phage display''
     vectors are a powerful tool for obtaining antigen-specific
     antibody fragments.  To date, this approach has been used to
     isolate abundant, but not rare, human autoantibodies of IgG class.  We
     have compared the relative efficiencies of panning pComb3 libraries made
     from intrathyroidal plasma cells for abundant human autoantibodies to
     thyroid peroxidase (TPO) and rare autoantibodies to the thyrotropin
     receptor (TSHR).  TPO-specific Fab were readily obtained from a library
     using three different forms of recombinant antigen, (i) purified
     TPO, (ii) impure TPO in culture medium and, (iii) TPO expressed on the
     surface of CHO cells.  In contrast, TSHR-specific Fab were not isolated.
     This was the case despite repeated pannings of six libraries from three
     optimal patients (IgG/kappa and IgG/lambda libraries for each patient).
     Both purified recombinant TSHR and CHO cells expressing TSHR on
     their surface were used.  Library enrichment was observed on some
     screenings.  However, Fab expressed by individual clones or from
     enriched libraries were not specific as determined by (i) binding to
     purified, radiolabeled antigen, (ii) FAGS analysis of TSHR on intact CHO
     cells and, (iii) inhibition of radiolabeled TSH binding.
     Remarkably, in screening for both TPO- and TSHR-specific Fab,
     neither library enrichment nor the retention of cDNA inserts of the
     correct size correlated with obtaining Fab with the antigenic specificity
     sought.  Indeed, excellent enrichment could be observed with conditioned
     medium from untransfected cells.  Our data suggest that the key to
     isolating rare antibodies from phage display libraries is not
     the creation of vast libraries of greater diversity or even the
     development of more stable vectors.  Rather, success in this endeavor
     appears to require reducing the ''noise'' of non-specific clones in a
     moderately sized library.

L12  ANSWER 2 OF 2     MEDLINE on STN
1993317610.    PubMed ID: 8327473.   Cloning from the thyroid of a protein
     related to actin binding protein that is recognized by Graves disease
     immunoglobulins. Leedman P J; Faulkner-Jones B; Cram D S; Harrison P J;
     West J; O'Brien E; Simpson R; Coppel R L; Harrison L C. (Burnet Clinical
     Research Unit, Walter and Eliza Hall Institute of Medical Research,
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Victoria, Australia.) Proceedings of the National Academy of Sciences of the United States of America, (1993 Jul 1) Vol. 90, No. 13, pp. 5994-8. Journal code: 7505876. ISSN: 0027-8424.
Report No.: NLM-PMC46853. Pub. country: United States. Language: English.

AB Human actin binding protein (ABP) links specific membrane glycoproteins to cytoskeletal actin microfilaments. In human platelets and leukocytes, ABP directly links, respectively, the membrane glycoproteins GPIb and the **high-affinity** Fc receptor for IgG (Fc gamma IR) to cytoskeletal actin microfilaments. Similar interaction between the thyrotropin (**TSH**) receptor and ABP in endocrine cells might explain the rapid and profound disruption of actin microfilaments induced by **TSH** in cultured thyroid follicular cells. By **screening** a thyroid lambda gt11 cDNA expression library with serum from a Graves disease patient, we identified a clone encoding a protein, designated truncated ABP (TABP), that shares extensive homology (approximately 70%) with ABP. TABP is a truncated ABP-like protein with an open reading frame of 195 aa that encodes a protein of approximately 21 kDa. TABP lacks an actin binding domain but contains two predicted beta-sheet repeats within which is a putative dimerization domain and between which lies a putative glycoprotein binding site containing a consensus site for phosphorylation by Ca(2+)-calmodulin kinase II. TABP contains a unique C-terminal insertion within which lies a hydrophobic predicted membrane-associated region, absent from ABP. Although TABP mRNA is expressed widely, immunoblot analysis demonstrated the presence of TABP **antibodies** specifically in the sera of a minority of subjects with autoimmune thyroid disease. A 24-residue sequence of similarity was identified between the **TSH** receptor and platelet glycoprotein GPIb alpha that may represent a transmembrane ABP binding site. We suggest, therefore, that signal transduction by **TSH** in the thyroid involves direct linkage of the **TSH** receptor to actin microfilaments by ABP and that TABP may interact with ABP to mediate **TSH**-induced actin microfilament disruption.

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=> s l1 and glycoforms
L13        104 L1 AND GLYCOFORMS

=> s l13 and human TSH
L14          0 L13 AND HUMAN TSH

=> s l13 and TSH
L15          6 L13 AND TSH

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16           2 DUP REMOVE L15 (4 DUPLICATES REMOVED)

=> d l16 1-2 cbib abs

L16  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
2005:823920   Document No. 143:244656  Process for screening
     glycoform-specific antibodies.  Ronin, Catherine; Donadio, Sandrine
     (Centre National de la Recherche Scientifique, Fr.; Universite de Provence
     Aix-Marseille 1).  PCT Int. Appl. WO 2005076013 A2 20050818, 83 pp.
     DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY,
     BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
     GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
     LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
     PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT,
     TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG,
     CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML,
     MR, NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.
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APPLICATION: WO 2005-EP1160 20050204. PRIORITY: EP 2004-290290 20040204.
AB The present invention relates to the use of the assessment of the binding between - antibodies elicited against a first glycoprotein, and - at least one glycoform of a second glycoprotein, said second glycoprotein being itself a glycoform of the first protein, wherein said glycoform of the second glycoprotein is selected from a group of **glycoforms** of the second glycoprotein, each glycoform of said group corresponding to a determined glycosylation state defined by a determined sialylation state, and/or a determined branching state, and/or a determined fucosylation state, provided that said glycosylation state is not uniquely defined by a substantially unsialylated state, for the **screening** of glycoform specific antibodies directed against a given glycoform of the second glycoprotein.

L16 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
2000225630. PubMed ID: 10762294. The development of a sialic acid specific lectin-immunoassay for the measurement of human chorionic gonadotrophin **glycoforms** in serum and its application in normal and Down's syndrome pregnancies. Abushoufa R A; Talbot J A; Brownbill K; Rafferty B; Kane J W; Robertson W R. (University of Manchester, Department of Clinical Biochemistry, Hope Hospital, Salford, UK.) Clinical endocrinology, (2000 Apr) Vol. 52, No. 4, pp. 499-508. Journal code: 0346653. ISSN: 0300-0664. Pub. country: ENGLAND: United Kingdom. Language: English.
AB OBJECTIVE: We have developed and validated a lectin-immunoassay for the recognition of sialic acid residues on hCG **glycoforms** in serum. DESIGN: This assay employs a hCG specific capture antibody and a sialic acid specific lectin (Wheat Germ Agglutinin) labelled with horse radish peroxidase. RESULTS: The standard curve covered hCG concentrations of 0-4000 IU/l (3rd IS for hCG, 75/537) with an analytical sensitivity of 1.0 IU/l. The within and between batch coefficient of variation was < 7% for all doses. Cross-reactivity of < 1% with **TSH**, LH, FSH, hCGalpha, hCGbeta and desialylated hCG confirmed assay specificity. Dilutions of serum of < 10% final concentration were parallel to the standard curve (within and between batch CV, < 6%). The assay working range was 100 - > 500 000 IU/l and the recovery of hCG from serum was in the range of 94.5% to 115.4%, with a mean value of 102.1%. The assay detected a time dependent change in hCG sialylation during normal pregnancy with the relative abundance of sialylated hCG declining after week 9 and increasing after week 15 of gestation. In addition preliminary studies showed that maternal serum hCG concentrations measured with the lectin-immunoassay were elevated in high risk Down's pregnancies (as defined by conventional **screening** tests between weeks 16-18 gestation, median multiple of median, 3.14; range 1.81-19.12, P < 0. 001) and low risk (1.57, 0.49-6.14, P = 0.034) compared to normal (1. 00, 0.32-3.20) pregnancies. Furthermore, the lectin immunoassay had greater discriminatory power compared to conventional immunoassay of hCG and hCGbeta between normal and both low and high risk Down's pregnancies. CONCLUSION: This assay will allow analysis of serum samples for the investigation of sialylated variants of hCG **glycoforms** in various pathological and physiological situations.

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=> s l1 and glycoprotein
L17      13711 L1 AND GLYCOPROTEIN

=> s l17 and recombinant human TSH
L18         11 L17 AND RECOMBINANT HUMAN TSH

=> s l18 and affinity
L19          0 L18 AND AFFINITY
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=> dup remove l18
PROCESSING COMPLETED FOR L18
L20 3 DUP REMOVE L18 (8 DUPLICATES REMOVED)

=> d l20 1-3 cbib abs

L20 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
2009547717. PubMed ID: 19592511. Small-molecule agonists for the thyrotropin receptor stimulate thyroid function in human thyrocytes and mice. Neumann Susanne; Huang Wenwei; Titus Steve; Krause Gerd; Kleinau Gunnar; Alberobello Anna Teresa; Zheng Wei; Southall Noel T; Inglese James; Austin Christopher P; Celi Francesco S; Gavrilova Oksana; Thomas Craig J; Raaka Bruce M; Gershengorn Marvin C. (Clinical Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892, USA.) Proceedings of the National Academy of Sciences of the United States of America, (2009 Jul 28) Vol. 106, No. 30, pp. 12471-6. Electronic Publication: 2009-07-10. Journal code: 7505876. E-ISSN: 1091-6490. Pub. country: United States. Language: English.

AB Seven-transmembrane-spanning receptors (7TMRs) are prominent drug targets. However, small-molecule ligands for 7-transmembrane-spanning receptors for which the natural ligands are large, heterodimeric **glycoprotein** hormones, like thyroid-stimulating hormone (TSH; thyrotropin), have only recently been reported, and none are approved for human use. We have used quantitative high-throughput **screening** to identify a small-molecule TSH receptor (TSHR) agonist that was modified to produce a second agonist with increased potency. We show that these agonists are highly selective for human TSHR versus other **glycoprotein** hormone receptors and interact with the receptor's serpentine domain. A binding pocket within the transmembrane domain was defined by docking into a TSHR homology model and was supported by site-directed mutagenesis. In primary cultures of human thyrocytes, both TSH and the agonists increase mRNA levels for thyroglobulin, thyroperoxidase, sodium iodide symporter, and deiodinase type 2, and deiodinase type 2 enzyme activity. Moreover, oral administration of the agonist stimulated thyroid function in mice, resulting in increased serum thyroxine and thyroidal radioiodide uptake. Thus, we discovered a small molecule that activates human TSHR in vitro, is orally active in mice, and could be a lead for development of drugs to use in place of **recombinant human TSH** in patients with thyroid cancer.

L20 ANSWER 2 OF 3 MEDLINE on STN DUPLICATE 2
2009536119. PubMed ID: 19509106. The p.A2215D thyroglobulin gene mutation leads to deficient synthesis and secretion of the mutated protein and congenital hypothyroidism with wide phenotype variation. Pardo Viviane; Vono-Toniolo Jussara; Rubio Ileana G S; Knobel Meyer; Possato Roberta F; Targovnik Hector M; Kopp Peter; Medeiros-Neto Geraldo. (Thyroid Unit (LIM 25), University of Sao Paulo Medical School, Av. Dr. Arnaldo 455-4A, Sao Paulo, SP, Brazil.) The Journal of clinical endocrinology and metabolism, (2009 Aug) Vol. 94, No. 8, pp. 2938-44. Electronic Publication: 2009-06-09. Journal code: 0375362. E-ISSN: 1945-7197. Pub. country: United States. Language: English.

AB CONTEXT: Thyroglobulin (TG) is a large **glycoprotein** and functions as a matrix for thyroid hormone synthesis. TG gene mutations give rise to goitrous congenital hypothyroidism (CH) with considerable phenotype variation. OBJECTIVES: The aim of the study was to report the genetic **screening** of 15 patients with CH due to TG gene mutations and to perform functional analysis of the p.A2215D mutation. DESIGN: Clinical evaluation and DNA sequencing of the TG gene were performed in all patients. TG expression was analyzed in the goitrous tissue of one patient. Human cells were transfected with expression vectors containing mutated and wild-type human TG cDNA. RESULTS: All

patients had an absent rise of serum TG after stimulation with **recombinant human TSH**. Sequence analysis revealed three previously described mutations (p.A2215D, p.R277X, and g.IVS30+1G>T), and two novel mutations (p.Q2142X and g.IVS46-1G>A). Two known (g.IVS30+1G/p.A2215D and p.A2215D/p.R277X) and one novel (p.R277X/g.IVS46-1G>A) compound heterozygous constellations were also identified. Functional analysis indicated deficiency in TG synthesis, reduction of TG secretion, and retention of the mutant TG within the cell, leading to an endoplasmic reticulum storage disease, whereas small amounts of mutant TG were still secreted within the cell system. CONCLUSION: All studied patients were either homozygous or heterozygous for TG gene mutations. Two novel mutations have been detected, and we show that TG mutation p.A2215D promotes the retention of TG within the endoplasmic reticulum and reduces TG synthesis and secretion, causing mild hypothyroidism. In the presence of sufficient iodine supply, some patients with TG mutations are able to compensate the impaired hormonogenesis and generate thyroid hormone.

L20 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

2009:836256 Small-molecule agonists for the thyrotropin receptor stimulate thyroid function in human thyrocytes and mice. Neumann, Susanne; Huang, Wenwei; Titus, Steve; Krause, Gerd; Kleinau, Gunnar; Alberobello, Anna Teresa; Zheng, Wei; Southall, Noel T.; Inglese, James; Austin, Christopher P.; Celi, Francesco S.; Gavrilova, Oksana; Thomas, Craig J.; Raaka, Bruce M.; Gershengorn, Marvin C. (Clinical Endocrinology Branch, National Institutes of Health, Bethesda, MD, 20892, USA). Proceedings of the National Academy of Sciences of the United States of America, Early Edition (July 10 2009), 1-6, 6 pp. (English) 2009. CODEN: PNASC8. URL: http://www.pnas.org/cgi/reprint/0904506106v1 Publisher: National Academy of Sciences.

AB Seven-transmembrane-spanning receptors (7TMRs) are prominent drug targets. However, small-mol. ligands for 7-transmembrane-spanning receptors for which the natural ligands are large, heterodimeric **glycoprotein** hormones, like TSH (TSH; TSH), have only recently been reported, and none are approved for human use. We have used quant. high-throughput **screening** to identify a small-mol. TSH receptor (TSHR) agonist that was modified to produce a second agonist with increased potency. We show that these agonists are highly selective for human TSHR vs. other **glycoprotein** hormone receptors and interact with the receptor's serpentine domain. A binding pocket within the transmembrane domain was defined by docking into a TSHR homol. model and was supported by site-directed mutagenesis. In primary cultures of human thyrocytes, both TSH and the agonists increase mRNA levels for thyroglobulin, thyroperoxidase, sodium iodide symporter, and deiodinase type 2, and deiodinase type 2 enzyme activity. Moreover, oral administration of the agonist stimulated thyroid function in mice, resulting in increased serum thyroxine and thyroidal radioiodide uptake. Thus, we discovered a small mol. that activates human TSHR in vitro, is orally active in mice, and could be a lead for development of drugs to use in place of **recombinant human TSH** in patients with thyroid cancer.

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